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The Human E3 $\alpha$  Ubiquitin Ligase Family

Inventors: Han et al.

Docket No.: 01017/35966B

Sheet 1 of 23 (Fig. 1A)

## Figure 1A

SEQ ID NO:

6	mouse_E3 $\alpha$ I	MASEMEPEVQ	AI D-RSLLEC	SAAEI AGRWL	QATDLNREVV	QHLAHCVPKI	49
4	human_E3 $\alpha$ I	MASELEPEVQ	AI D-RSLLEC	SAAEI AGKWL	QATDLTREVV	QHLAHYVPKI	49
15	mouse_E3 $\alpha$ I	MADEEMDGAE	RMDVSPPEPPL	APQRPASWMD	QQVDFYTAFL	HHLAQLVPEI	50
2	human_E3 $\alpha$ I	MADEEAGGTE	RMEISAEELPQ	TPQRLLASWMD	QQVDFYTAFL	HHLAQLVPEI	50
Consensus							
	MA. E. . . . .	D. . . . .	L. . . . .	A. . . W.	Q. . D. . . . .	HLA. . VP. I	50
6	mouse_E3 $\alpha$ I	YCRGPNPFPQ	KEDTLAQHIL	LGPM <del>E</del> W <sup>W</sup> IC <sup>A</sup>	EDPALGF <sup>P</sup> KL	EQANKPSHLC	99
4	human_E3 $\alpha$ I	YCRGPNPFPQ	KEDMLAQHVL	LGPM <del>E</del> W <sup>W</sup> L <sup>C</sup> <sup>G</sup>	EDPAFGF <sup>P</sup> KL	EQANKPSHLC	99
15	mouse_E3 $\alpha$ I	YFAEMDPDLE	KQEESVQMSI	LTPLEWWLFG	EDPDI CLEKL	KHSG-AFQLC	99
2	human_E3 $\alpha$ I	YFAEMDPDLE	KQEESVQMSI	FTPLEWWLFG	EDPDI CLEKL	KHSG-AFQLC	99
Consensus							
	Y. . . . .	P. . . . .	K. . . . .	Q. . . . .	L. P. EWYL. G	EDP. . . . . KL	LC 100
6	mouse_E3 $\alpha$ II	GRVFKVGEPT	YSCRDCAVDP	TCVL <sup>C</sup> ME <sup>C</sup> FL	GSI HRDHRYR	MTTSGGGGFC	149
4	human_E3 $\alpha$ II	GRVFKVGEPT	YSCRDCAVDP	TCVL <sup>C</sup> ME <sup>C</sup> FL	GSI HRDHRYR	MTTSGGGGFC	149
15	mouse_E3 $\alpha$ II	GKVF <sup>K</sup> SGETT	YSCRDCAI DP	TCVL <sup>C</sup> MDCFQ	SSVHKNHRYK	MHTSTGGGF <sup>C</sup>	149
2	human_E3 $\alpha$ II	GKVF <sup>K</sup> SGETT	YSCRDCAI DP	TCVL <sup>C</sup> MDCFQ	DSVHKNHRYK	MHTSTGGGF <sup>C</sup>	149
Consensus							
	GRVFK. GE. T	YSCRDCAI. DP	TCVL <sup>C</sup> CM CF.	. S. H. . HRY.	M. TS. GGGFC	150	
6	mouse_E3 $\alpha$ II	DCGDTEAWKE	GPYCQKHKLS	SSEVVEEDP	LVHLSEDVI A	RTYNI FAI MF	199
4	human_E3 $\alpha$ II	DCGDTEAWKE	GPYCQKHELN	TSEI <sup>E</sup> EEEDP	LVHLSEDVI A	RTYNI FAI TF	199
15	mouse_E3 $\alpha$ II	DCGDTEAWKT	GPF CVDHEPG	RAGTTKESLH -	CPLNEEVIA	QARRI FPSVI	198
2	human_E3 $\alpha$ II	DCGDTEAWKT	GPF CVNHEPG	RAGTI KENSR -	CPLNEEVIV	QARKI FPSVI	198
Consensus							
	DCGDTEAWK.	GP. C. . HE. . . . .	E. . . . .	L. E. VI A . . . . .	I F. . . . .	200	

Figure 1B

## Figure 1C

6	mouse_E3 $\alpha$ II	SSLVDRLLN	DSKLWKGARS	VYHQLFMSL	LMDLKYYKKLF	ALRFAKNYRQ	398
4	human_E3 $\alpha$ II	SSLVDRLLS	DSKLWKGARS	VYHQLFMSL	LMDLKYYKKLF	AVRFAKNYQQ	398
15	mouse_E3 $\alpha$ I	PCLISRLMLW	DAKLYKGARK	ILHELI FSSF	FMEMEYKKLF	AMEFVKYYKQ	398
2	human_E3 $\alpha$ I	PCLISRLMLW	DAKLYKGARK	ILHELI FSSF	FMEMEYKKLF	AMEFVKYYKQ	398
	Consensus	... L.. RLM.	D. KL. KGAR.	... H. L.. SS.	... M... YKKLF	A. . F. K. Y. Q	400
6	mouse_E3 $\alpha$ II	LQRDFM <del>E</del> DDH	ERAVSVTALS	VQFFTAPTLA	RMLLTENLM	TVI I KAFMDH	448
4	human_E3 $\alpha$ II	LQRDFM <del>E</del> DDH	ERAVSVTALS	VQFFTAPTLA	RMLI TEENL	M SII I KTFMDH	448
15	mouse_E3 $\alpha$ I	LQKEYISDDH	ERSISITALS	VQMLTVPTLA	RHLI EEQNVI	SVI TETLLEV	448
2	human_E3 $\alpha$ I	LQKEYISDDH	DRSISITALS	VQMFTVPTLA	RHLI EEQNVI	SVI TETLLEV	448
	Consensus	LQ. . . . DDH	ER. . S. TALS	VQ. FT. PTLA	R. LI. E. N.	SVI . . T. . .	450

**Figure 1D**

SEQ ID NO:	6	mouse_E3 $\alpha$ II	LKHRDAQGRF	QFERYTALQA	FKFRVQSLI	LDLKVVLI SK	PTEWSDELRQ	498
	4	human_E3 $\alpha$ II	LRHRDAQGRF	QFERYTALQA	FKFRVQSLI	LDLKVVLI SK	PTEWSDELRQ	498
	15	mouse_E3 $\alpha$ I	LPEYLDRNN-	KFN-FQGYSQ	DKLGRVYAVI	CDLKYLISK	PVIWTERLRA	496
	2	human_E3 $\alpha$ I	LPEYLDRNN-	KFN-FQGYSQ	DKLGRVYAVI	CDLKYLISK	PTIWTERLRM	496
		Consensus	L.....	F.....	K..RV...	DLKY.LISK	PT.W..LR.	500
	6	mouse_E3 $\alpha$ II	KFLQGFDNFL	ELLKCMQGMD	PITRQVGQHI	EMEPEWEAAF	TLQMKLTHVI	548
	4	human_E3 $\alpha$ II	KFLEGFDNFL	ELLKCMQGMD	PITRQVGQHI	EMEPEWEAAF	TLQMKLTHVI	548
	15	mouse_E3 $\alpha$ I	QFLEGFRSFL	KILTCTMQGME	EIRRQVGQHI	EVDPDWAAI	AIQMQLKNI L	546
	2	human_E3 $\alpha$ I	QFLEGFRSFL	KILTCTMQGME	EIRRQVGQHI	EVDPDWAAI	AIQMQLKNI L	546
		Consensus	.FLEGF..FL	..L.CMQGM	.I.RQVGQHI	E..P.WEAA.	..QM.L...	550
	6	mouse_E3 $\alpha$ II	SMVQDWICALD	EKVLI EAYKK	CLAVLTOCHG	GFTDGEQPI T	LSICGHSVET	598
	4	human_E3 $\alpha$ II	SMMQDWICASD	EKVLI EAYKK	CLAVLMQCHG	GYT DGEQPI T	LSICGHSVET	598
	15	mouse_E3 $\alpha$ I	LMFQEWACD	EDLLLVAYKE	CHKAVMRCST	NFMSSTKTV-	VQLCGHSLET	595
	2	human_E3 $\alpha$ I	LMFQEWACD	EELLLVAYKE	CHKAVMRCST	SFISSSKTV-	VQSCGHSLET	595
		Consensus	M.Q.WCA:DE..	L..:AYK	C..:M.C..	F..:..	CGHS.ET	600

## Figure 1E

6	mouse_E3 $\alpha$ II	I RYCVSQEKV SI HLPISRLL AGLHVLLSKS EVAYKFPELL PLSELSPPM <del>L</del>	648
4	human_E3 $\alpha$ II	I YCVSQEKV SI HLPVSRLL AGLHVLLSKS EVAYKFPELL PLSELSPPM <del>L</del>	648
15	mouse_E3 $\alpha$ I	KSYKVS <del>ED</del> LV SI HLP <del>S</del> RTL AGLHVRLSRL GAI SRLHEFV PFD <del>S</del> QVEVL	645
2	human_E3 $\alpha$ I	KSYRV <del>SE</del> DLV SI HLP <del>S</del> RTL AGLHVRLSRL GAVSRLHEFV SFEDFQVEVL	645
	Consensus	.. Y. VS. . . V SI HLP. SR. L AGLHV. LS. . . . . E. . . P. . . . . L	650
6	mouse_E3 $\alpha$ II	I EHPLRCLVL CAQVHAGMMR RNGFSSLVNQI YYYHNVKCRR EMFDKDI VML	698
4	human_E3 $\alpha$ II	I EHPLRCLVL CAQVHAGMMR RNGFSSLVNQI YYYHNVKCRR EMFDKDVVM <del>L</del>	698
15	mouse_E3 $\alpha$ I	VEYPLRCLVL VAQVVAEMMR RNGLSSLISQV FYYQDVVKCRE EMYDKDI I ML	695
2	human_E3 $\alpha$ I	VEYPLRCLVL VAQVVAEMMR RNGLSSLISQV FYYQDVVKCRE EMYDKDI I ML	695
	Consensus	. E. PLRCLVL . AQV. A. MMR RNG. SL. . Q. . YY.. VKCR. EM DKDI . ML	700
6	mouse_E3 $\alpha$ II	QTGVSMMDPN HFLM <del>M</del> LSRF ELYQLFSTPD YGKRFSSSEVT HKD <del>V</del> VQQNNT	748
4	human_E3 $\alpha$ II	QTGVSMMDPN HFLM <del>M</del> LSRF ELYQI FSTPD YGKRFSSSEI T HKD <del>V</del> VQQNNT	748
15	mouse_E3 $\alpha$ I	QI GASI MDPN KFLLLVLQRY EL. . . . TDA FNKTIS. - K DQDLI KQYNT	738
2	human_E3 $\alpha$ I	QI GASL MDPN KFLLLVLQRY EL. . . . AEA FNKTIS. - K DQDLI KQYNT	738
	Consensus	Q. G. S. MDPN . FL. . . L. R. EL. . . T. . . K. . S. . . . D. . . Q. NT	750

Figure 1F

6	mouse_E3 $\alpha$ II	LI EEMLYLI	ML VGERFNG	VGQVAATDEI	KREI I HQLSI	KPMASHSELVK	798
4	human_E3 $\alpha$ II	LI EEMLYLI	ML VGERFSPG	VGQVNATDEI	KREI I HQLSI	KPMASHSELVK	798
15	mouse_E3 $\alpha$ I	LI EEMQVL	YI VGERYVPG	VGNVTREEVI	MREI THLLCI	EPMPHSAI AR	788
2	human_E3 $\alpha$ I	LI EEMQVL	YI VGERYVPG	VGNVTKEEVT	MREI I HLLCI	EPMPHSAI AK	788
	Consensus	LI EEM...I	YGER..PG	VG.V....I	.REI I H.L.I	.PM HS...K	800
6	mouse_E3 $\alpha$ II	SLPEDENKET	GME SVI EAVA	HFKKPGLTGR	GMYELKPECA	KEFNL YFYHF	848
4	human_E3 $\alpha$ II	SLPEDENKET	GME SVI EAVA	HFKKPGLTGR	GMYELKPECA	KEFNL YFYHF	848
15	mouse_E3 $\alpha$ I	NLPEENNNT	GLENVI NKVA	TFKKPGVSGH	GYYELKDESL	KDFNMWYHY	838
2	human_E3 $\alpha$ I	NLPEENNNT	GLENVI NKVA	TFKKPGVSGH	GYYELKDESL	KDFNMWYHY	838
	Consensus	.LPE. EN. ET	G. E. VI .. VA	.FKKPG. . G.	G. YELK. E..	K. FN. YFYH.	850
6	mouse_E3 $\alpha$ II	SRAEQSKAEE	AQRKLKRENK	EDT ALPPP AL	PPFCPLFASL	VNI LQCDVML	898
4	human_E3 $\alpha$ II	SRAEQSKAEE	AQRKLKRQNR	EDT ALPPP VL	PPFCPLFASL	VNI LQS DVML	898
15	mouse_E3 $\alpha$ I	SKTQHSKAEH	MQKKRRKQEN	KDE ALPPP PP	PEFCPAFSKV	VNL LSCDVM	888
2	human_E3 $\alpha$ I	SKTQHSKAEH	MQKKRRKQEN	KDE ALPPP PP	PEFCPAFSKV	I NLL NCDI MM	888
	Consensus	S...SKAE.	.Q. K...Q..	D. ALPPP..	P. FCP. F...	VN. L. CDVM	900

## Figure 1G

SEQ ID NO:	mouse_E3 $\alpha$ II	human_E3 $\alpha$ II	mouse_E3 $\alpha$ I	human_E3 $\alpha$ I	mouse_E3 $\alpha$	human_E3 $\alpha$	Consensus
6	YI MGT I LQWA VEHHGSAWSE	YI MGT I LQWA VEHHGSAWSE	SM QRVL HLI	GMAL QEEKHH	LEN AVE GHVQ	948	
4	CI MGT I LQWA VEHNGYAWSE	CI MGT I LQWA VEHNGYAWSE	SM QRVL HLI	GMAL QEEKQH	LEN VTE EHVV	948	
15	YI LRT I FERA VDTE SNL WTE	YI LRT I FERA VDTE SNL WTE	GML QMAF HIL	AL GL LEE KQQ	LQKA PEE EV-	937	
2	YI LRT VFERA I DTD SNL WTE	YI LRT VFERA I DTD SNL WTE	GML QMAF HIL	AL GL LEE KQQ	LQKA PEE EV-	937	
	YI . . . . A V . . . . W E	YI . . . . A V . . . . W E	ML Q . . . H .	ML Q . . . H .	ML . E E KQ . L . . A . E E . V .	950	
6	TFTFTQK I SK PGDAPHNSPS	TFTFTQK I SK PGDAPHNSPS	I LAM L E TLQ N	APS L E AH KDM	I RW L K M F N A	998	
4	AFDFYHKAS R	AFDFYHKAS R	PGEAPKNSPS	I LAM L E TLQ N	APY L E V HKDM	I RW L K T F N A	998
15	TFDFYHKAS R	TFDFYHKAS R	I QM L L E RLK G	I PQ L E G Q KDM	I T W L Q M F D T	987	
2	TFDFYHKAS R	TFDFYHKAS R	I QM L L E RLK G	I PQ L E G Q KDM	I T W L Q M F D T	984	
	TF. F . . K. S . . G . . . N . .	TF. F . . K. S . . G . . . N . .	I . . . L E . L . .	I . . . L E . L . .	. P. L E . . K D M I . W L. M F . .	1000	
6	I KK I RE -- CS	I KK I RE -- CS	SSSPVVAE A G	T I M E E S S R D K	DKA E R K R K A E	I A R L R R E K I M	1046
4	VKKM R E -- SS	VKKM R E -- SS	PTSPV A E T E G	T I M E E S S R D K	DKA E R K R K A E	I A R L R R E K I M	1046
15	VKRLREKSCL	VKRLREKSCL	VVATTSGLEC	I KSE E I T H D K	EKA E R K R K A E	A A R L H R Q K I M	1037
2	VKRLREKSCL	VKRLREKSCL	I VATTSGSES	I K N D E I T H D K	EKA E R K R K A E	A A R L H R Q K I M	1034
	VK . . RE . . C . . . . . E .	VK . . RE . . C . . . . . E .	EE . . . . . E .	EE . . . . . E .	EE . . . . . E .	EE . . . . . E .	
					KA E R K R K A E	AR L . R . K I M	1050

## Figure 1H

6	mouse_E3 $\alpha$ II	AQMSEMQRFHF	DENKELFQQ	TLELDTASAA	TL--	DSSPPV	SDAALTALGP	1094
4	human_E3 $\alpha$ II	AQMSEMQRFHF	DENKELFQQ	TLELDASTSA	VL--	DHSPPVA	SDMFLTALGP	1094
15	mouse_E3 $\alpha$ I	AQM <del>S</del> ALQKNF	ETHKL <del>M</del> DN	TSEVTGKEDS	MEEEESTSAV	SEASRIALGP	1087	
2	human_E3 $\alpha$ I	AQM <del>S</del> ALQKNF	ETHKL <del>M</del> DN	TSEMPGKEDS	MEEEESTPAV	SDYSRIALGP	1084	
	Consensus	AQM <del>S</del> ..Q..F	...K....	T.E.....	....S.P.V	SD....ALGP	1100	
6	mouse_E3 $\alpha$ II	AQTQVPEPRQ	FVTCILCQEE	QEVTVGSRAM	VLAAFVQRST	VLSKDRTKTI	1144	
4	human_E3 $\alpha$ II	TQTQVPEQRQ	FVTCILCQEE	QEVKVESRAM	VLAAFVQRST	VLSKNRSKFI	1144	
15	mouse_E3 $\alpha$ I	KRGPAVTEKE	VLTCILCQEE	QEVKLENNAM	VLSACVQKST	ALTQHRGKPV	1137	
2	human_E3 $\alpha$	KRGPSVTEKE	VLTCILCQEE	QEVKIENNAM	VLSACVQKST	ALTQHRGKPI	1134	
	Consensus	.....	..TCILCQEE	QEVK.E..AM	VLA.VQ.ST	.L...R.K.I	1150	
6	mouse_E3 $\alpha$ II	AD-PEKYDPL	FMHPDLSCGT	HTGSCGGHVMH	AHCWQRYFDS	VQAKEQRRQQ	1193	
4	human_E3 $\alpha$ II	QD-PEKYDPL	FMHPDLSCGT	HTSSCGHI	MH	AHCWQRYFDS	VQAKEQRRQQ	1193
15	mouse_E3 $\alpha$ I	DHLGETLDPL	FMDPDLAHGT	YTGSCGGHVMH	AVCWQKYFEA	VQ---LSSQQ	1184	
2	human_E3 $\alpha$ I	ELSGEALDPL	FMDPDLAYGT	YTGSCGGHVMH	AVCWQKYFEA	VQ---LSSQQ	1181	
	Consensus	...E.DPL	FM PDL..GT	.TGSCGGHVMH	A.CWQ.YF..	VQ.....QQ	1200	

## Figure 1I

6	mouse_E3 $\alpha$ II	RLRLHTSYDV	ENGEGFLCPLC	ECLSNTVIPL	L-LPPRSILS	RRLN-FSDQP	1241
4	human_E3 $\alpha$ II	RLRLHTSYDV	ENGEGFLCPLC	ECLSNTVIPL	L-LPPRNIFN	NRLN-FSDQP	1241
15	mouse_E3 $\alpha$ I	RIHVDL-FDL	ESGEYFLCPLC	KSLCNTVIPI	IPLQPQKINS	ENAEALAQLL	1233
2	human_E3 $\alpha$ I	RIHVDL-FDL	ESGEYFLCPLC	KSLCNTVIPI	IPLQPQKINS	ENADALAQLL	1230
	Consensus	R.....D.	E.GE.LCPLC	..L.NTVIP.	..L.P..I.S	.....	1250
6	mouse_E3 $\alpha$ II	DLAQWTRAVT	QQIKVVQMLR	RKHNAADTS	SSEDTEAMNI	IPIPEGFRPD	1290
4	human_E3 $\alpha$ II	NLTQWRTIS	QQIKALQFLR	KEESTP-NNA	STKNSENVDE	LQLPEGFRPD	1290
15	mouse_E3 $\alpha$ I	TLARWQTVL	ARI SGYNIKH	AKGEAAPAVPV	LFNQGMGDST	FEFHSLSF	1283
2	human_E3 $\alpha$ I	TLARWQTVL	ARI SGYNIRH	AKGENP-IPI	FFNQGMGDST	LEFHSLSF	1279
	Consensus	.LA.W.TV.	..I.....	.K...P...	.....	.....	1300
6	mouse_E3 $\alpha$ II	FYPRNPYSDS	I KEMLTTFGT	AAYKVGKVKH	PNEGDPRVPI	LCWGTCAVTI	1340
4	human_E3 $\alpha$ II	FRPKIPYSES	I KEMLTTFGT	ATYKVGKVKH	PNEEDPRVPI	MCWGS CAYTI	1340
15	mouse_E3 $\alpha$ I	VQSSVKYSNS	I KEMWILFAT	TIYRIGLKVP	PDELDPRVPM	MFWSTCAFTI	1333
2	human_E3 $\alpha$ I	VESSI KYSNS	I KEMWILFAT	TIYRIGLKVP	PDERDPRVPM	LTWSTCAFTI	1329
	Consensus	.....YS.S	I KEM...F.T	..Y..GLKV.	P.E.DPRVP.	..W.TCA.TI	1350

Figure 1J

SEO ID NÖ

6	mouse_E3 $\alpha$ II	QSIERILSDE	EKPVFGPLPC	RDDCLRSLT	RFAAAHWTVA	LLPVQGHFC	1390
4	human_E3 $\alpha$ II	QSIERILSDE	DKPLFGPLPC	RDDCLRSLT	RFAAAHWTVA	SVSVQGHFC	1390
15	mouse_E3 $\alpha$ I	QAIENLLGDE	GKPLFGALQN	RQHSGLKALM	QFAVAQRATC	PQVLIHKHLA	1383
2	human_E3 $\alpha$ I	QAIENLLGDE	GKPLFGALQN	RQHNGLKALM	QFAVAQRITC	PQVLIQKHLV	1379
Consensus		Q . IE . . L . DE	KPLFG . L . .	R . . . L . . L .	. FA . A . . . .	. . . . Q . H . .	1400
6	mouse_E3 $\alpha$ II	KLFASLVPSD	SYEDLPCILD	IDMFHLLVGL	VLAFTPALQCQ	D---FSGSSL	1437
4	human_E3 $\alpha$ II	KLFASLVPND	SHEELPCILD	IDMFHLLVGL	VLAFTPALQCQ	D---FSGISL	1437
15	mouse_E3 $\alpha$ I	RLLSVILPNL	QSENTPGLLS	VDLFHVVLVGA	VLAFTPPLYWD	DTVDLQPSPL	1433
2	human_E3 $\alpha$ I	RLLSVWLPNI	KSEDTPCLLS	IDLFHVVLVGA	VLAFTPPLYWD	DPVDLQPSSV	1429
Consensus		L . . . . PN .	... E . . PC . L .	ID. FH. LVG .	VLAFTP . L . .	D . . . . SSL	1450
6	mouse_E3 $\alpha$ II	ATG--DLHIF	HLVTMAHIVQ	ILLTSCTEEN	---GMDQENP	TGEEELAILS	1482
4	human_E3 $\alpha$ II	GTG--DLHIF	HLVTMAHIIQ	ILLTSCTEEN	---GMDQENP	PCEEESAVLA	1482
15	mouse_E3 $\alpha$ I	SSSYNHLYLF	HLITMAHMLQ	ILLTTDTDSL	PGPPLAEGEE	DSEEARCASA	1483
2	human_E3 $\alpha$ I	SSSYNHLYLF	HLITMAHMLQ	ILLTVDTGL-	---PLAQVQE	DSEEAEHSASS	1475
Consensus		... . . . L . . F	HL. TMAH . . Q	ILLT . . T . . .	--- . . . Q . . .	EE . . . . .	1500

## Figure 1K

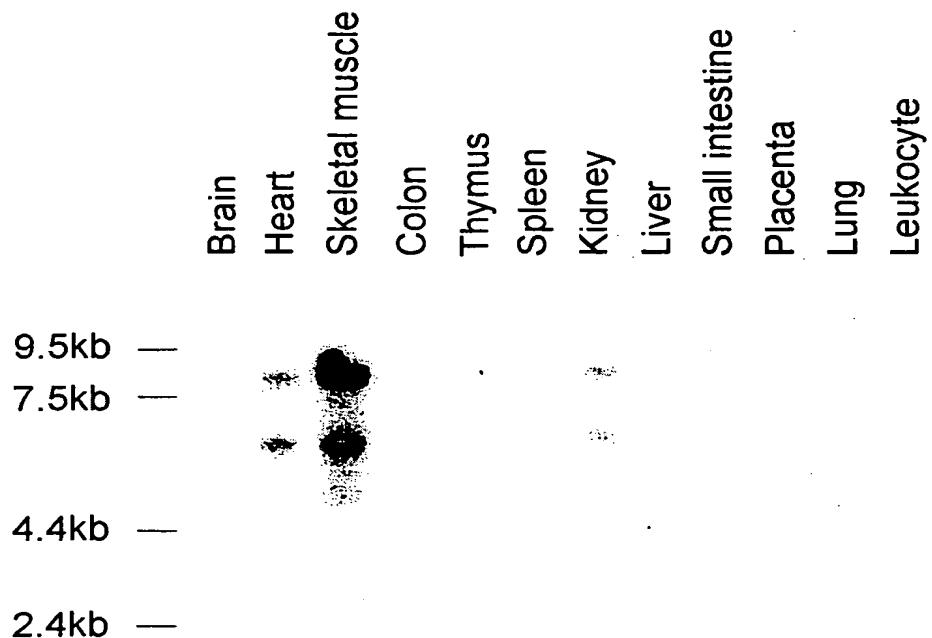
6	mouse_E3 $\alpha$ II	LHKTLHQYTG	SALKEAPSGW	HLWRSVRAAI	MPFLKCSAL	FHYLNGVPAP	1532
4	human_E3 $\alpha$ II	LYKTLHQYTG	SALKEIPSGW	HLWRSVRAGI	MPFLKCSALF	FHYLNGVPSP	1532
15	mouse_E3 $\alpha$ I	FFVEVSOHTD	GLTGCAGAPGW	YLWLSLRNGI	TPYLRCAAALL	FHYLLGVAPP	1533
2	human_E3 $\alpha$ I	FFAEISQYTS	GSIGCDIPGW	YLWVSLKNGI	TPYLRCAAALF	FHYLLGVTPPP	1525
Consensus		.....QYT.	.....GW	.....GW	.....GW	P. L. C. ALF	FHYL. GV.. P 1550
6	mouse_E3 $\alpha$ II	PDLQV-SGTS	HFEHILCNYLS	LPTNLHLFQ	ENSDIMNSLI	ESWCQNSEVK	1581
4	human_E3 $\alpha$ II	PDIQV-PGTS	HFEHILCSYLS	LPNNLICLFQ	ENSEIMNSLI	ESWCRNSEVK	1581
15	mouse_E3 $\alpha$ I	EELFANSAEG	EFSALCSYLS	LPTNLFLLFQ	EYWDTIRPLL	QRWCGDPALL	1583
2	human_E3 $\alpha$ I	EELHTNSAEG	EYSALCSYLS	LPTNLFLLFQ	EYWDTVRPLL	QRWCADPALL	1575
Consensus		..L...S...	.F..LCSYLS	LPTNL..LFQ	E...D...L...	WC.....	1600
6	mouse_E3 $\alpha$ II	RYLNGERGAI	SYPRGANKLI	DLPEDYSSLI	NQASNFSCP	SGGDKSRAPT	1631
4	human_E3 $\alpha$ II	RYLEGERDAI	RYPRESNKL	NLPEDYSSLI	NQASNFSCP	SGGDKSRAPT	1631
15	mouse_E3 $\alpha$ I	KSLKQKSAVV	RYPRKRNSLI	ELPEDYSCLL	NQASHFRCPR	SADDERKHPV	1633
2	human_E3 $\alpha$ I	NCLKQKNTVV	RYPRKRNSLI	ELPDDYSCLL	NQASHFRCPR	SADDERKHPV	1625
Consensus		..L.....	RYPR..N.LI	LPEDYS..L.	NQAS..F..CP.	S...D....P.	1650

## Figure 1L

6	mouse_E3 $\alpha$ II	LCLVCGSLLC	SQS YCCQAEI	E GEDV GACTA	HTY SCGSGAG	I F L RVRECQV	1681
4	human_E3 $\alpha$ II	LCLVCGSLLC	SQS YCCQTEL	E GEDV GACTA	HTY SCGSGVG	I F L RVRECQV	1681
15	mouse_E3 $\alpha$ I	LCLFCGAI LC	SQNI CCQE I V	NGEEVGACVF	HAL HCGAGVC	I F L KI RECRV	1683
2	human_E3 $\alpha$ I	LCLFCGAI LC	SQNI CCQE I V	NGEEVGACI F	HAL HCGAGVC	I F L KI RECRV	1675
	Consensus	LCL. CG. . LC	SQ. . CCQ. .	GE. VGAC. .	H. . CG. GV. .	I F L. . REC. V	1700
6	mouse_E3 $\alpha$ II	LFLAGKTKGC	F Y S P P Y L D D Y	GET D Q G L R R G	N P L H L C Q E R F	R K I Q K L W Q Q H	1731
4	human_E3 $\alpha$ II	LFLAGKTKGC	F Y S P P Y L D D Y	GET D Q G L R R G	N P L H L C K E R F	K K I Q K L W H Q H	1731
15	mouse_E3 $\alpha$ I	V L V E G K A R G C	A Y P A P Y L D E Y	GET D P G L K R G	N P L H L S R E R Y	R K L H L V W Q Q H	1733
2	human_E3 $\alpha$ I	V L V E G K A R G C	A Y P A P Y L D E Y	GET D P G L K R G	N P L H L S R E R Y	R K L H L V W Q Q H	1725
	Consensus	... . . . . . . . . . .	GC . Y . . PYLD. Y	GET D. GL. RG	N P L H L. . E R.	R K. . . . W Q Q H	1750
6	mouse_E3 $\alpha$ II	S I T E E I	G H A Q	E A N Q T L V G I	D W Q H L		1755
4	human_E3 $\alpha$ II	S V T E E I	G H A Q	E A N Q T L V G I	D W Q H L		1755
15	mouse_E3 $\alpha$ I	C I I E E I	A R S Q	E T N Q M L F G F N	W Q L L		1757
2	human_E3 $\alpha$ I	C I I E E I	A R S Q	E T N Q M L F G F N	W Q L L		1749
	Consensus	. I . E E I . . . .	Q E. N Q. L. G. .	W Q. L			1774

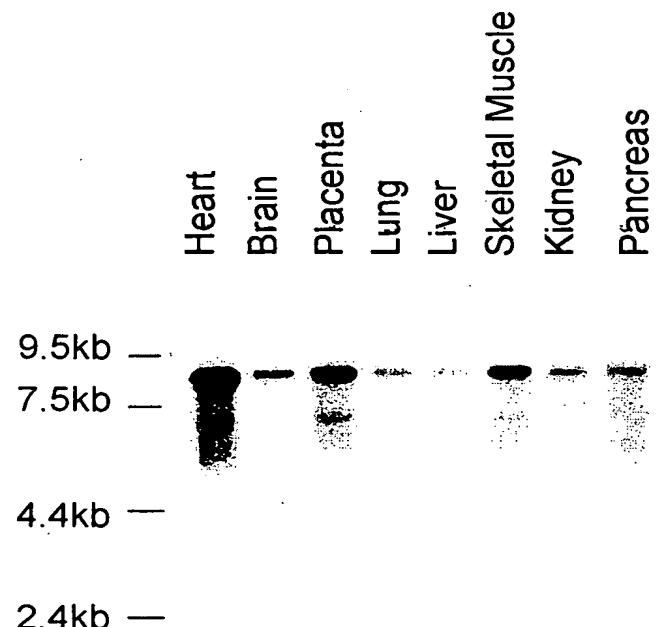
## FIG. 2

### Tth Expression Profile of huE3 $\alpha$ -II in Human Tissues

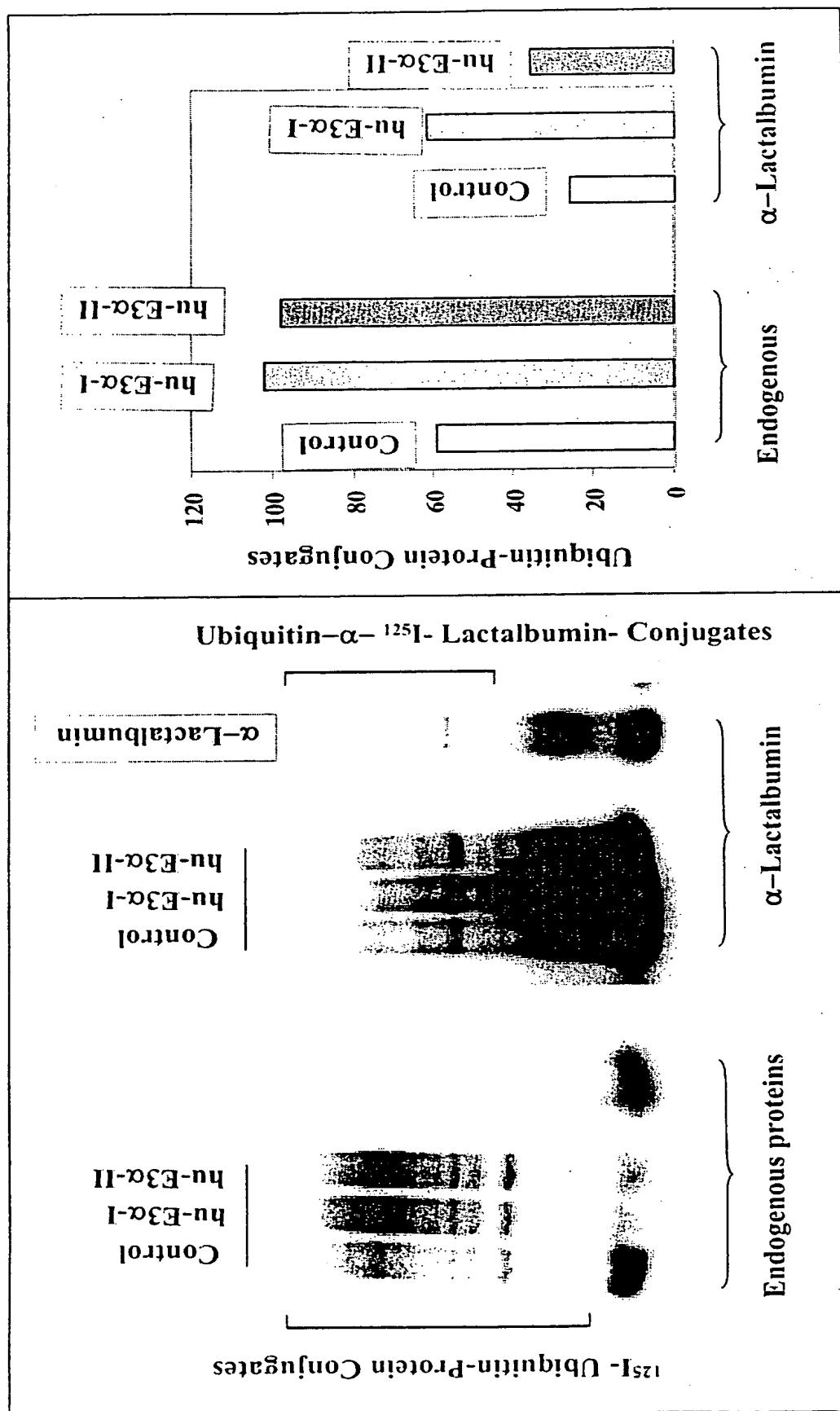


## FIG. 3

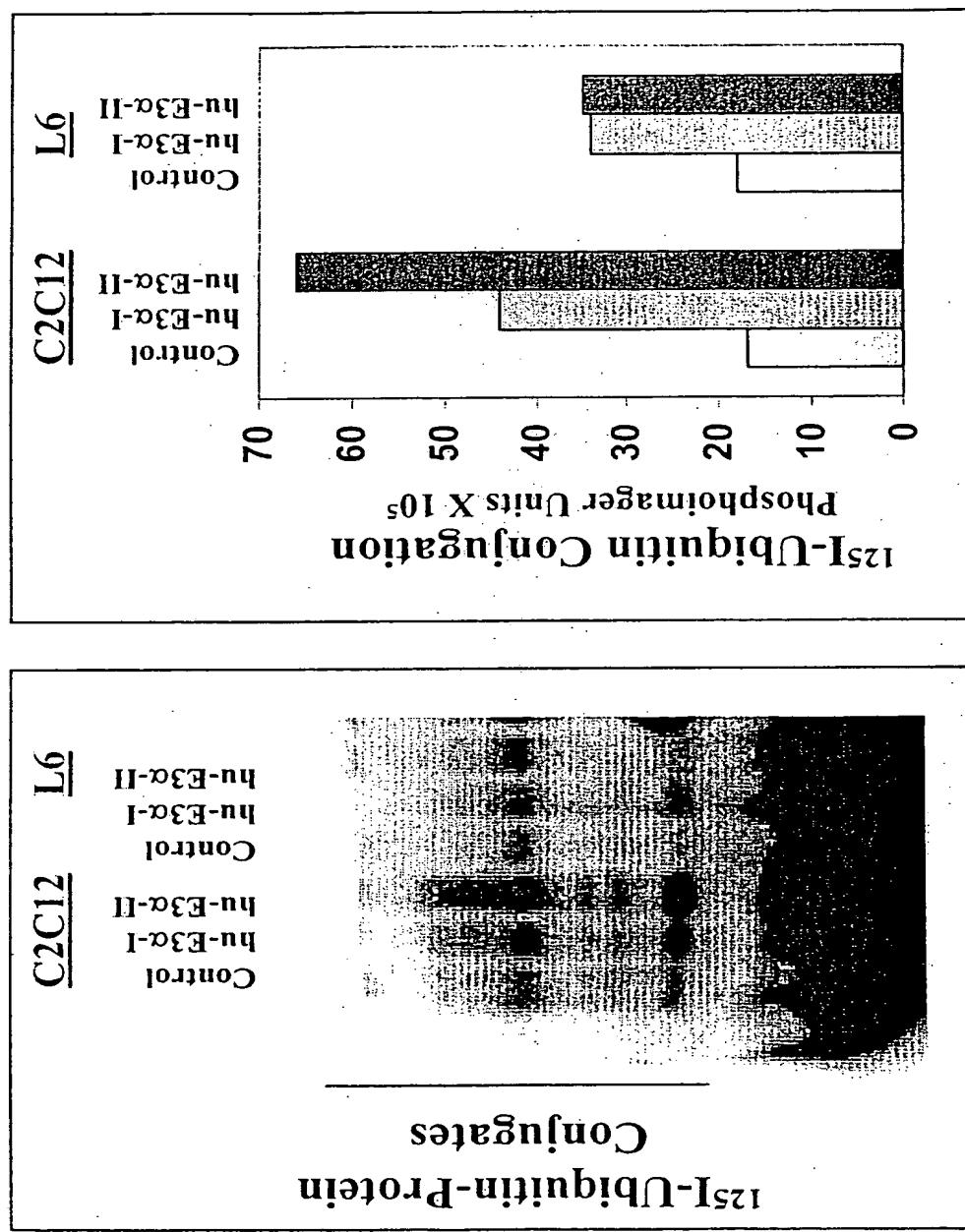
### Tth Expression Profile of huE3 $\alpha$ -I in Human Tissues



**Figure 4**  
**Ubiquitination of Endogenous Proteins**



**Figure 5**  
**Transfection of Human E3a-I or E3a-II cDNA Stimulates  
Ubiquitin Conjugation in Cultured Muscle Cell Lines**

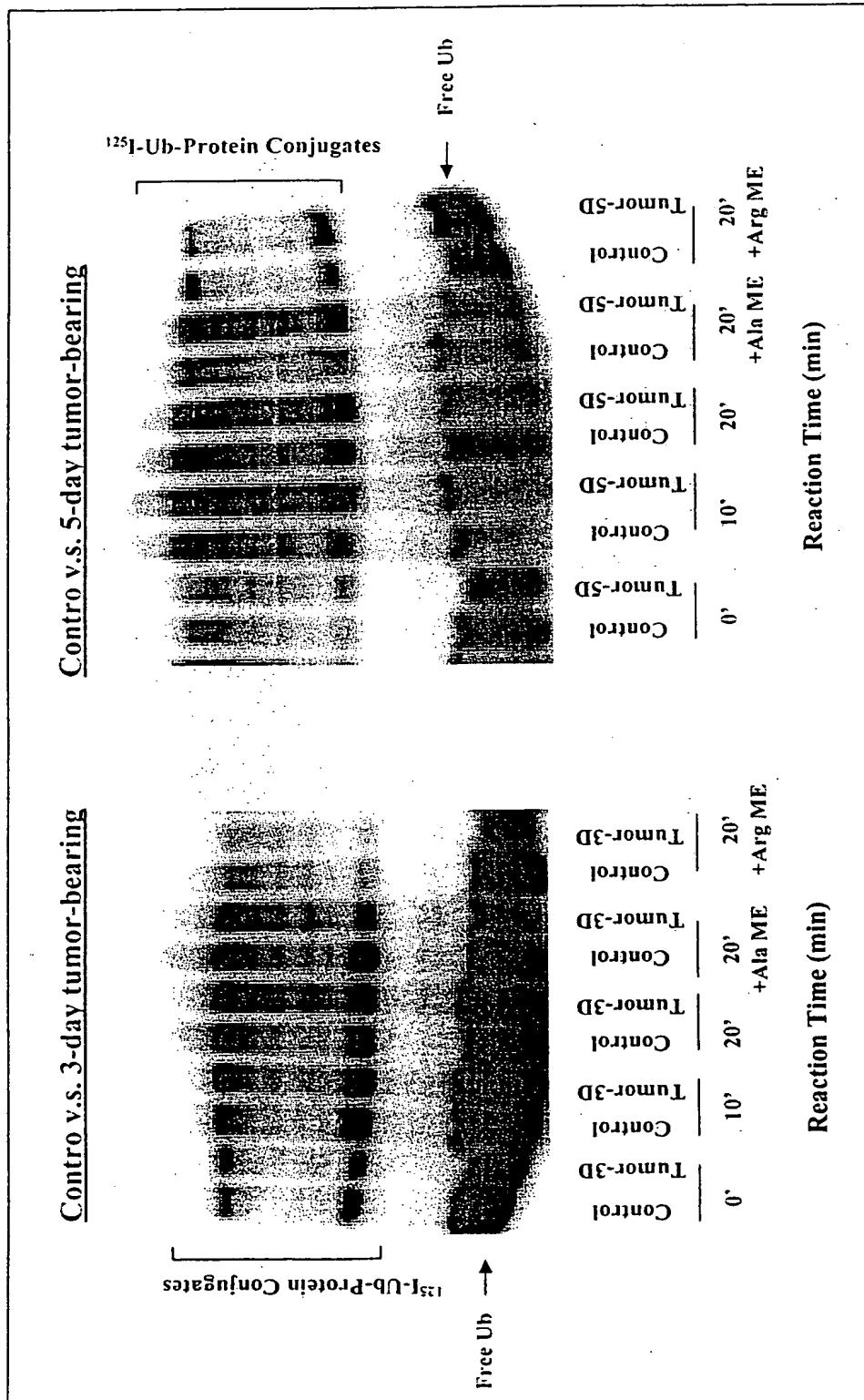


**Figure 6**

**125I-Ubiquitin Conjugation to Muscle Proteins and Its Sensitivity to E3 $\alpha$  Inhibitor in Skeletal Muscle Extracts**

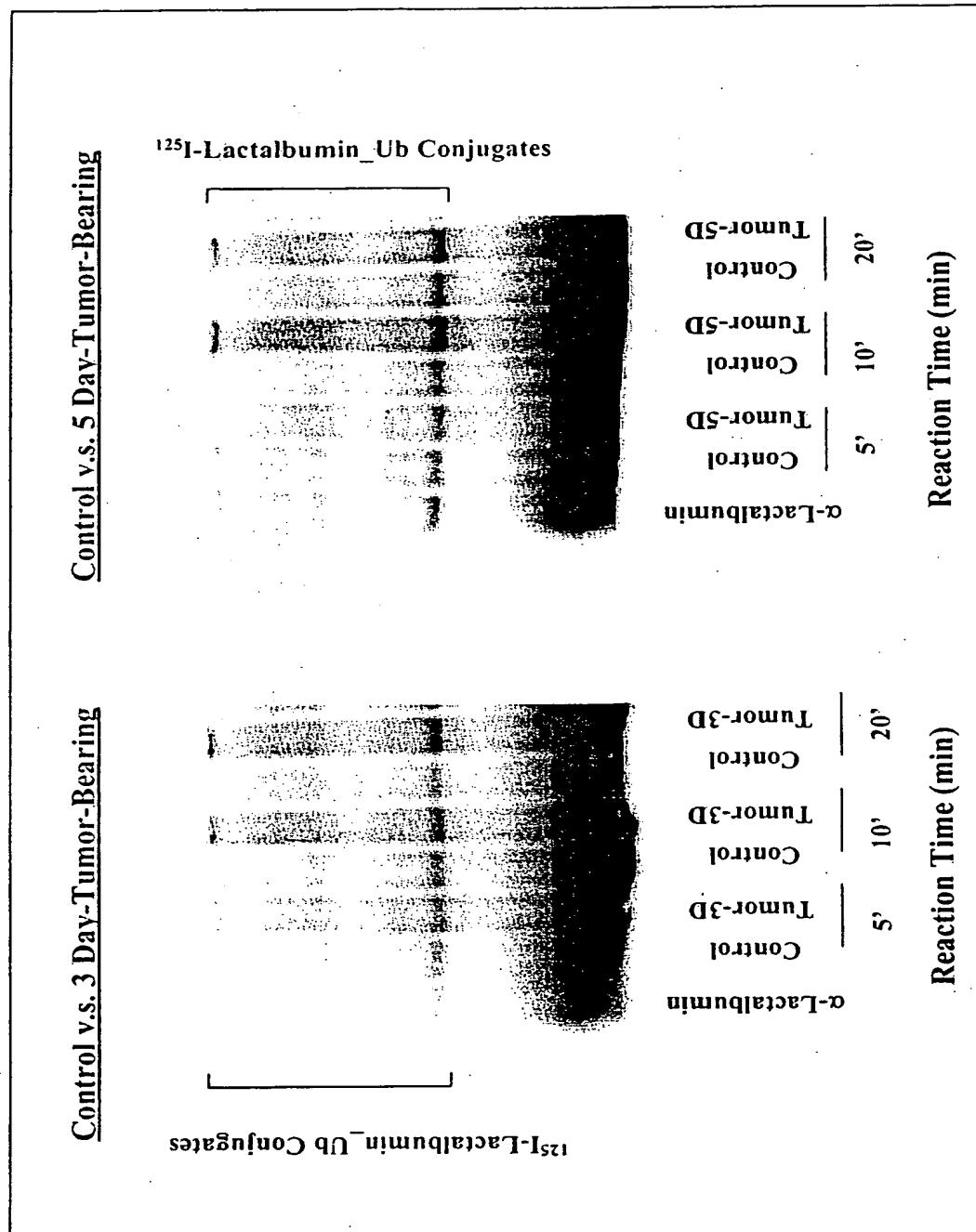
Control v.s. 3-day tumor-bearing

Control v.s. 5-day tumor-bearing



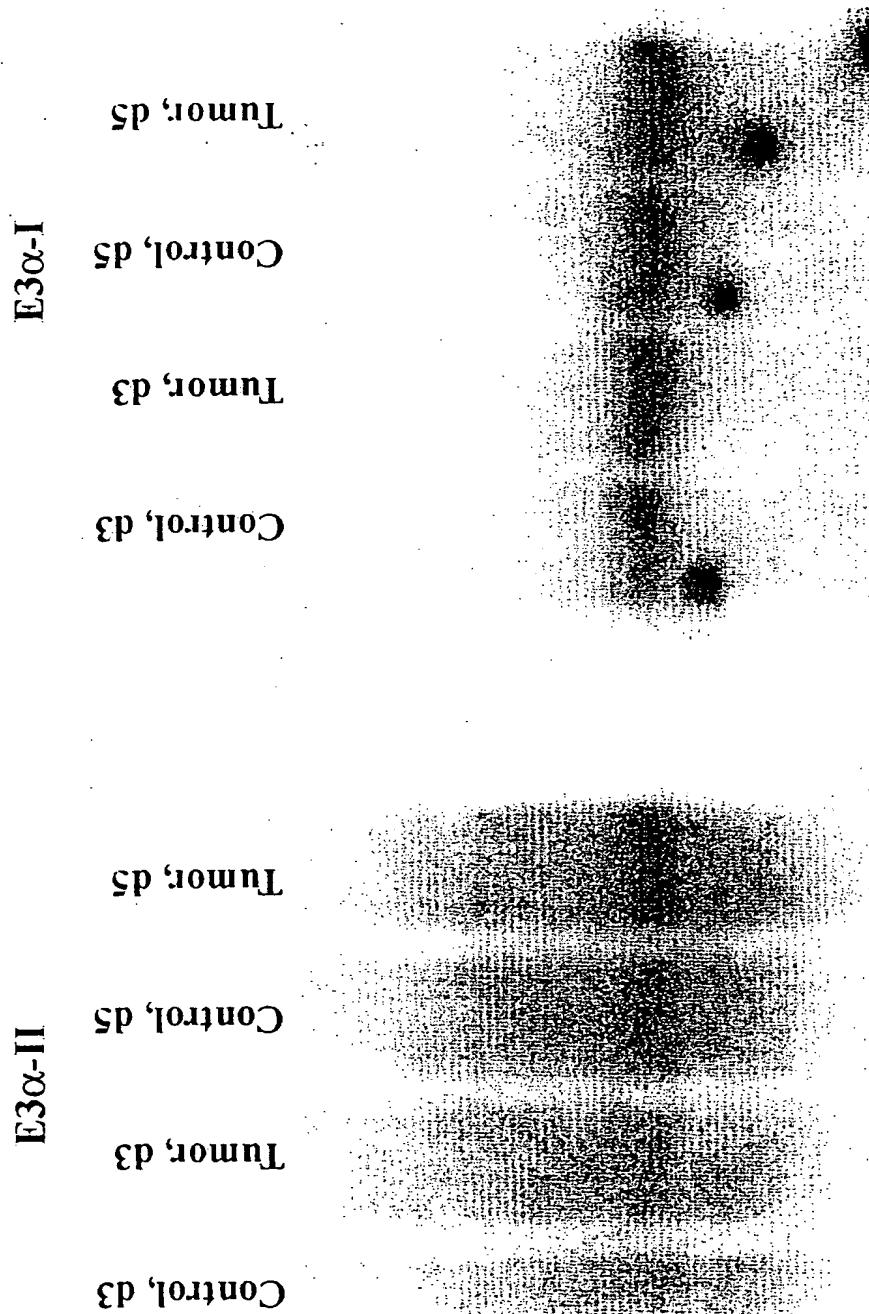
**Figure 7**

**Rates of Ubiquitination of N-end Rule Substrate  
 $\alpha$ -Lactalbumin in Skeletal Muscle Extracts**



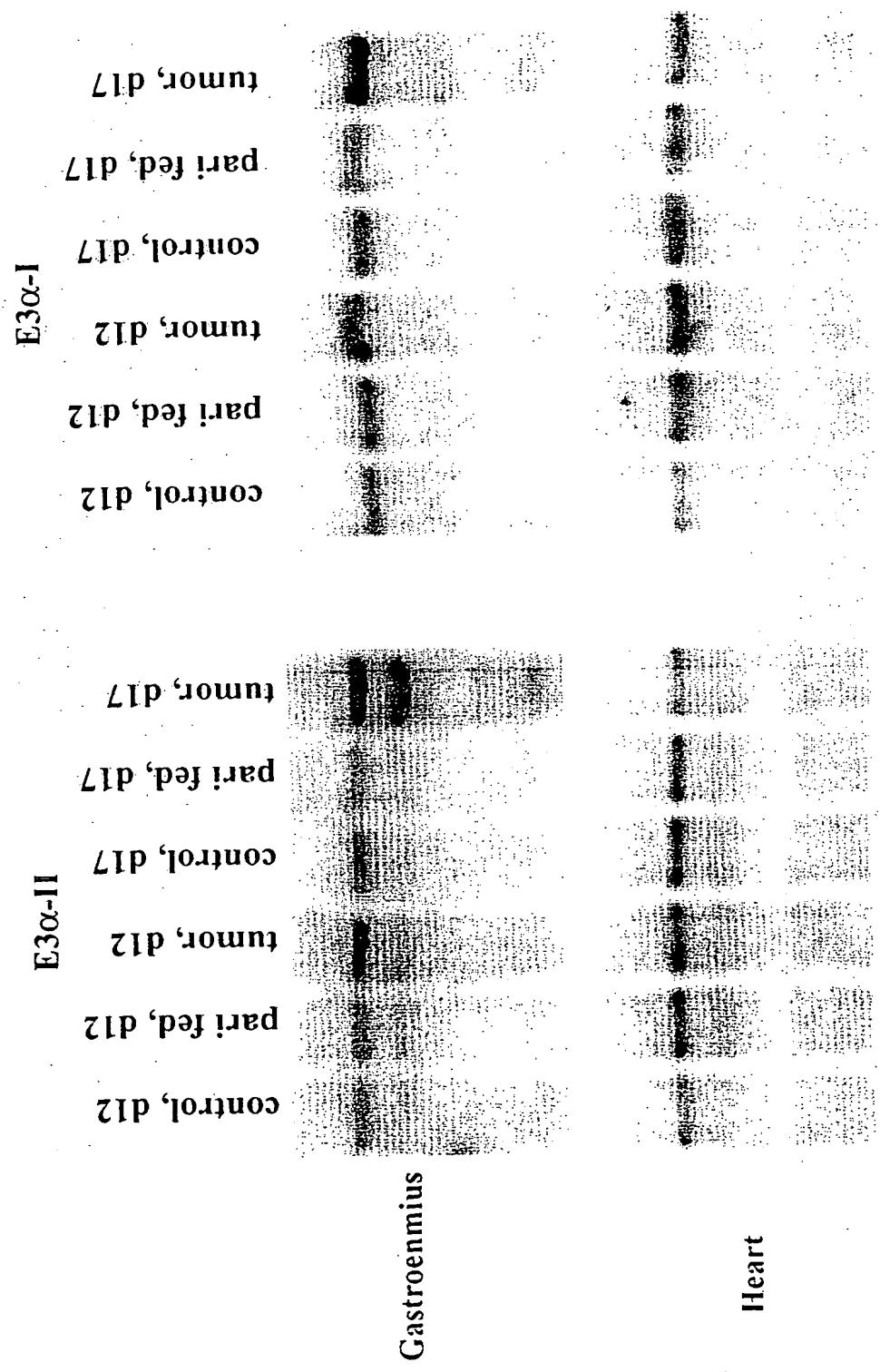
**Figure 8**

**Northern blot analysis of E3 $\alpha$ -I & E3 $\alpha$ -II expression  
in gastrocnemius muscles in YAH-130 experimental cachexia model**



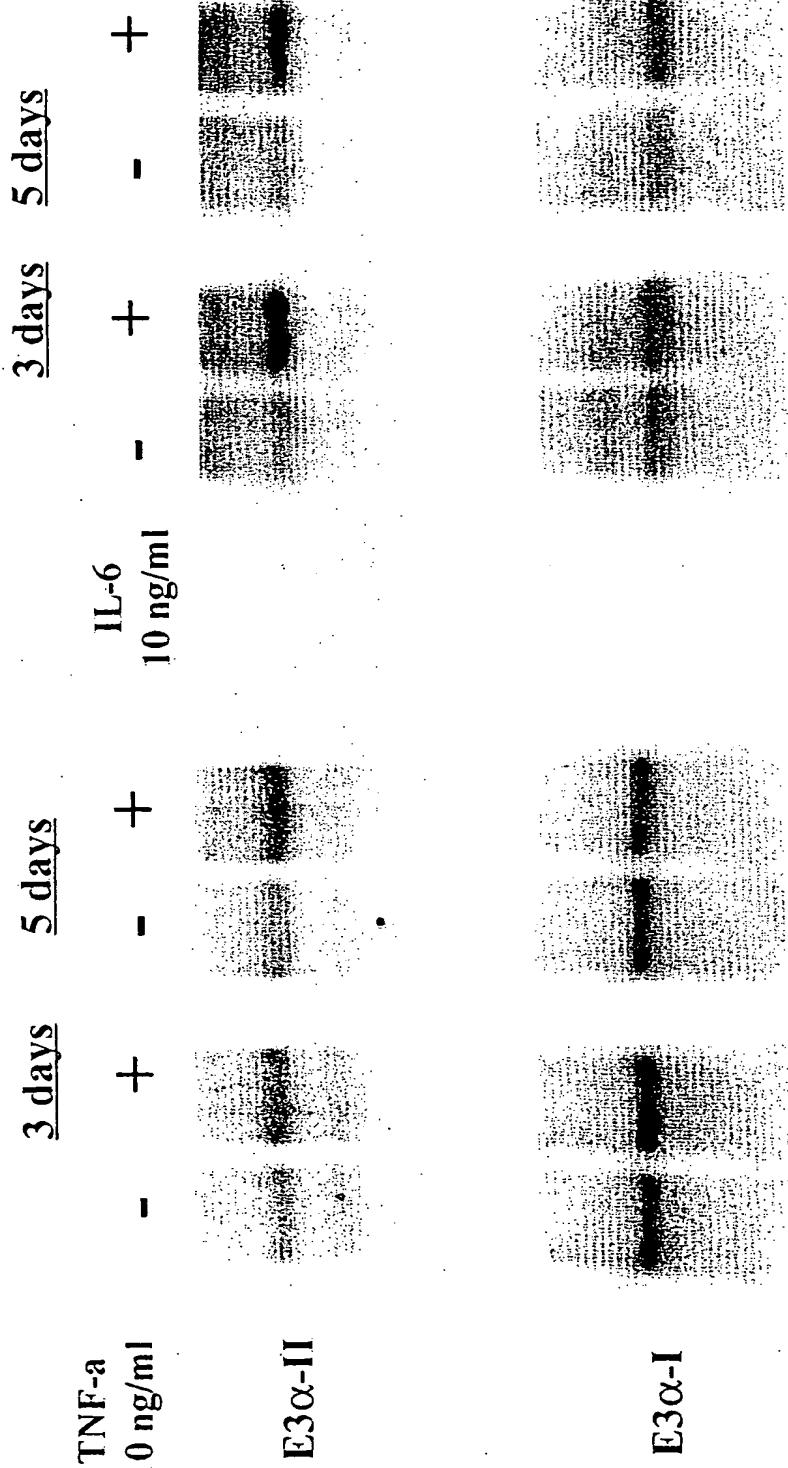
**Figure 9**

**Northern blot analysis of E3 $\alpha$ -I and E3 $\alpha$ -II expression in  
gastrocnemius muscle and cardiac muscle  
in C26 experimental cachexia model**

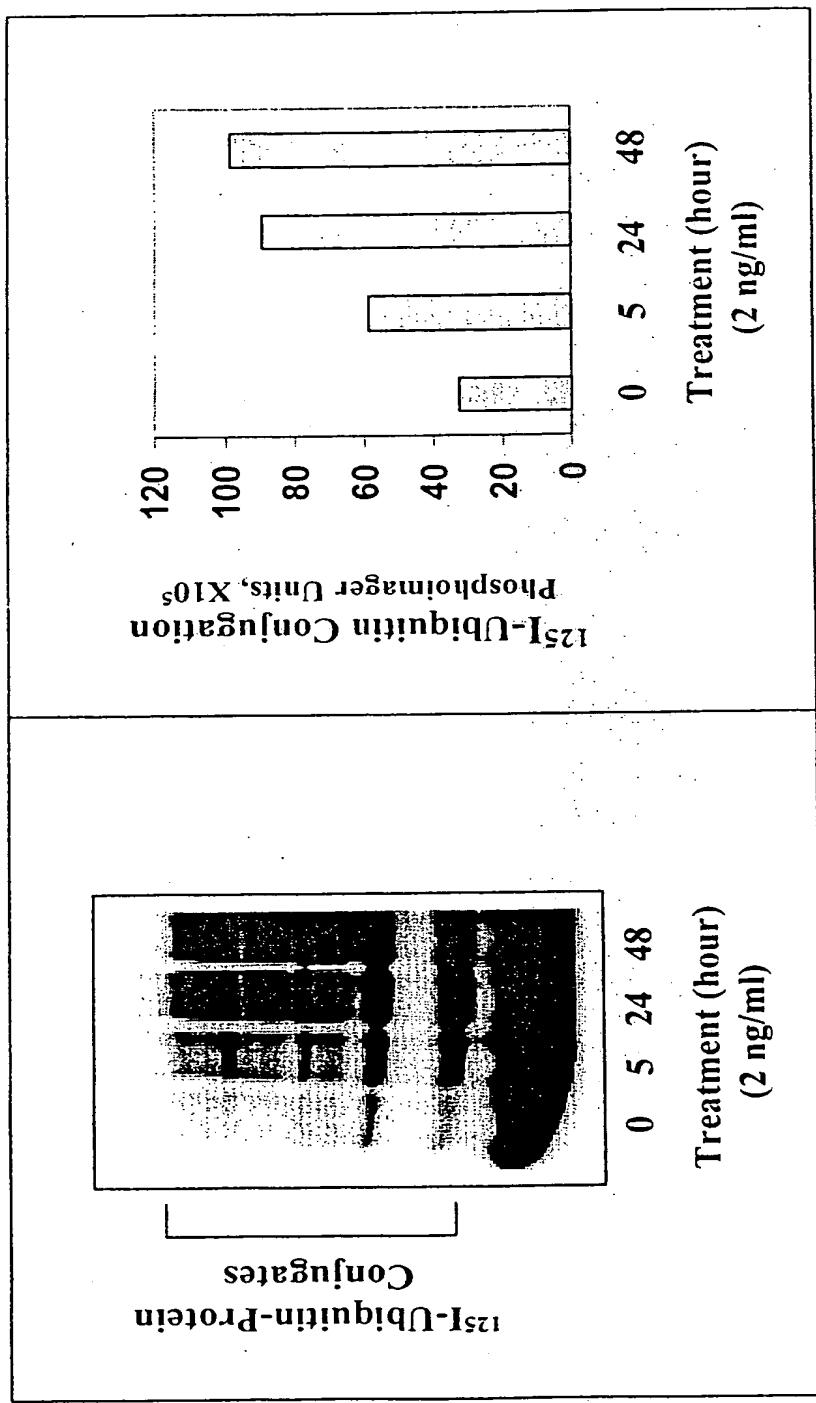


**Figure 10**

Proinflammatory cytokines TNF- $\alpha$  and IL-6 induce E3 $\alpha$ -III Expression in C2C12 myostube culture



**Figure 11**  
**IL-6 Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures**



**Figure 12**  
**TNF $\alpha$  Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures**

